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"Studies on the Physiology of Appetite"

SUMMARY

The basic factors responsible for the sensations which have to do with hunger and appetite have never been clearly understood. Smyth et al (1) have found that intravenously administered amino acids ("Amigen," Mead, Johnson or "Parenamine," Stearns) produced a decrease in the voluntary food intake in human subjects roughly consistent with the caloric content in the case of Amigen, but greater than the caloric intake in the case of Parenamine.

Briefly, our purposes in this study were to obtain data from animals on the influence of parenteral and intragastric instillation of various materials on the voluntary intake of food and to correlate with these data the coincident changes in blood and urine chemistry.

METHODS

Six healthy adult mongrel dogs were used in these studies. Each was confined in a separate metabolism cage from which the 24-hour output of urine could be collected daily. Each dog was allowed a period of four to twelve weeks for adjustment and for stabilization of his food intake.

The animals were fed once daily. The daily food intake was determined by offering each animal a carefully weighed 2 kg. portion of cubed horse meat, and allowing a standard 20 minute interval before removing the uneaten portion which was again weighed. The difference in weight was recorded as the voluntary food intake for the day.

When it was hoped that maximal stabilization had been attained, each animal was given an intravenous or intragastric

injection of one of the solutions to be tested daily for five days. When blood samples were required they were taken from a leg vein shortly before, midway (in some instances), and at the end of each injection.

The dog to be injected was removed from his cage and placed upon a table where he was supported in a standing position by a muslin hammock for the duration of the injection (usually two hours or more). He was then returned to his cage and fed, either immediately (21 experiments) or three hours later (25 experiments). Precautions against loss of urine during the time of transfer from and to the cage were not always successful and occasionally some urine was unavoidable lost on the floor. This difficulty accounts for some of the omissions in the chemical data. In order to reduce this type of accident to a minimum, the dogs were not routinely weighed as was originally intended. However, all dogs were weighed at the beginning and end of the study. There has been no evidence of weight loss, but rather of gain during the time of the recorded observations.

AVERAGE FOOD INTAKE

Besides the initial control period, the dogs were allowed several weeks rest between injection periods in most instances. The daily food intake during the control periods was not consistent and even the average daily food intake per week showed a considerable variation at times. Some dogs refused to eat on certain days. These voluntary fasting periods amounted in the averages for all dogs to 0.2 days out of five during the control periods.

INTRAVENOUS AMINO ACIDS

Amigen (Mead, Johnson): Each animal was given 200 or 250 cc. of Amigen intravenously once a day for five consecutive days. The material was injected slowly over a period of about two hours. In one such series (5 experiments on 5 dogs), the animal was returned to his cage and offered food as soon as the injection was completed. In another series (6 experiments on 5 dogs), feeding was delayed for three hours.

A significant decrease occurred in the average daily food intake of every dog in the first group during the five day injection period and continued for at least two days after the injections were stopped. The food intake of three of the dogs was less during the two days following the injection period than during that period; in two it was slightly greater. The daily average of all five dogs for the week, including the five day injection period and the two days following, was no

greater than during the five injection days alone. This shows not only a lack of compensation for the previously reduced intake of the first five days, but a persistence of the depressant effect of the injection for at least forty-eight hours.

The six experiments in which the dog was fed three hours after being returned to his cage presented a parallel situation. Again a decrease in the daily intake was noted except in Dog 1A in which there was little change from the previous two weeks but this was followed by a definite increase during the following two weeks. The daily average for the two days following the injections was again less than the daily average food intake during the injection period.

VUJ Mixture (Merck and Co.*) Each of five dogs was given 250 cc of an 8% solution of synthetic amino acids in water and the dog was fed immediately just as in the first Amigen series. A decrease in the average daily food intake was again noted. In this series, Dog 5 was considerably affected by the injection with vomiting and little or no intake of food during the four of the first five days of the injections. Since only one other dog in this series ate nothing on only one occasion, the decrease in the average daily intake for the group is perhaps exaggerated.

It will be noted that two of the five dogs again ate less during the two days following the injection period than during the five days of injection.

Parenamine series: A 6% amino acid solution known as Parenamine (Frederick Stearns and Co.) was given in a manner similar to the VUJ series. All dogs in the series showed a decrease in the average daily food intake during the injection period as compared with the preceding and following weeks.

The decrease in food intake persisted beyond the five day injection in this series as it did in the two amigen series, and to some extent in the VUJ series.

Merck's 6R7794: 200 or 250 cc. of a 10% mixture of amino acids (6R7794) were given in the same way as the VUJ series. There were no essential differences noted in the results when compared with the VUJ series.

5% Glucose series: 500 cc. of 5% glucose in distilled water were given intravenously and the dogs were immediately fed. These injections were given on the same plan as the others. All showed some depression in the daily average food intake during the injection period.

* A mixture of synthetic amino acids excluding glutamic acid.

Persistence of the decreased food intake for two days following the five day injection period is again noted, and an average of all dogs shows that less was eaten per day in the last two days following the injections than during the injection period.

Physiological Saline series: The procedure was the same as in the experiments described previously. The animals received 500 cc. of 0.9% saline solution intravenously, and were fed either immediately or (in three experiments) three hours later, A moderate decrease in the food intake during the injection period occurred also in this series. It was definitely less marked than when amino acids or dextrose was used.

INTRAGASTRIC INJECTIONS

Amigen: Each of four dogs was provided with a tubulated fistula according to the method of Thomas (2). After recovery from the operation and a rest period of two weeks injections were made into the stomach through a 16 gauge needle which was inserted through the cork stopper of the fistula tube. A 250 cc. volume of 10 per cent Amigen was instilled during a period of about one hour. The dog was then fed three hours later.

Only one animal showed a significant change in food intake during the injection period and this one took more food daily than during the preceding or the following two weeks.

BLOOD AND URINE CHEMISTRY AND NITROGEN BALANCE

The state of nitrogen balance during each of the various experimental procedures is indicated in Table II. These data may be summarized as follows:

(1) The N balance was generally negative during periods of decreased food intake incident to intravenous injection of glucose solutions.

(2) With intravenous NaCl solution, depression of food intake was accompanied by a significantly negative N balance in only one instance, in which the N intake was decreased considerably.

(3) Depression of food intake during intravenous injection of Parenamine was accompanied by either no change or a slightly negative N balance.

(4) There was no significant alteration in N balance during periods of intragastric instillation of Amigen except in one instance in which the food intake was depressed; in this case, the balance became slightly negative.

(5) A consistently positive N balance was maintained during periods of depressed food intake incident to intravenous administration of Amigen or VUJ mixture, even in those instances in which the N intake was markedly diminished and the caloric intake fell below suboptimal levels.

COMMENT.

It was noted during these experiments that the rectal temperature tended to rise during the intravenous injection. Although these changes were slight, and it is known that the dog's body temperature is quite labile, some experiments are being continued with closer attention to asepsis, and using pyrogen free materials where possible.

Table I

Percent Change in Food Intake During 5 Days of Parenteral Feedings.

Average of all Dogs	Intravenous 0.9% saline	Intravenous amigen: dog fed immed.	Intravenous amigen: dog fed in 3 hr	Intravenous VUJ: dog fed immed.	Intravenous parenamine: dog fed in 3 hr.	Intravenous 6R7794: dog fed in 3 hr	Intravenous glucose: dog fed in 3 hr	Intragastric amigen: dog fed in 3 hr
Percent change compared to preceding control period.	-29.1	-59.0	-36.4	-49.5	-32.7	-52.0	-42.4	+33.4
Percent change compared to following control period.	-32.6	-46.5	-39.1	-43.8	-29.4	-54.5	-44.4	+5.5

Continued

Table II
Nitrogen Balance

Treatment	Dog	1	2	3	4A	4B	5
10% Amigen IV (Fed immed.)	N intake*	8.06	5.04	3.80	5.73		4.26
	N output*	4.85	3.63	3.73	5.60		2.10
	N balance*	+3.21	+1.41	+0.07	+0.13		+2.16
10% Amigen IV (Fed 3 hr. later)	N intake	7.96	5.14	3.93	6.46	6.30	2.92
	N output	7.24	4.18	2.80	3.96	5.40	1.57
	N balance	+0.72	+0.96	+1.13	+2.50	+0.90	+1.45
10% Amigen (Intragastric)	N intake		3.86	5.79		12.40	5.65
	N output		4.66	6.14		12.25	5.88
	N balance		-0.80	-0.35		+0.15	-0.23
8% Amino Acids IV (VUJ)	N intake	5.55	4.76	6.44			5.36
	N output	4.45	3.82	6.34			5.18
	N balance	+1.10	+0.94	+0.10			+0.18
Parenamine	N intake	5.37 4.65	4.99	3.80			
	N output	6.00 4.66	5.71	3.42			
	N balance	+0.63 +0.06	-0.72	+0.38			
5% Glucose	N intake	3.74	4.58		3.64		2.82
	N output	1.76	7.75		6.38		3.65
	N balance	+2.02	-3.17		-2.74		-0.83
0.9% Saline	N intake	5.27	2.94	3.70			
	N output	5.30	4.38	3.42			
	N balance	-0.03	-1.44	+0.28			

*All Nitrogen values expressed in grams per day per kilogram body weight (estimated).

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References

1. Symth, C. J., Moyer, C. A., and Laischak, A. G. : Proc. Central. Soc. Clin. Research 18: 59, 1945.

2. Thomas, J. E.: Proc. Soc. Exp. Biol. and Medl 46: 260, 1946.

3. Friedman, M. H. F., and Bennett, I. F.: Fed. Proc. 2: 13, 1943.

4. Allison, J. B., J. A. Anderson and R. D. Seeley: Am. Chem. Soc. Abstract of 109 Meeting, p. 2A, No. 2, 1946.

5. Stevenson, G., P. P. Swanson, W. Willman and M. Brush: Fed. Proc. 5: 240, 1946.

6. Croft, P. B., and R. A. Peters: Nature 155: 175, 1945.

7. Glynn, L. E., H. P. Himsworth and A. Neuberger: Brit. J. Exper. Path. 26: 326, 1945.

8. Albanese, A. A., L. E. Holt, Jr., V. Irby and J. E. Brumbach, Jr.: J. Biol. Chem. 165: 179, 1946.

9. Elman, R., H. Davey and Y. Loo: Arch Biochem. 3: 45, 1945.

10. Sahyun, M., Kade, C. F., and J. Houston: Am. J. Digest. Dis. 14: 230, 1947.

11. Kozoll, D. D., W. S. Hoffman, and K. A. Meyer: Arch. Surg. 51: 59, 1945.

12. Elman, R., and D. O. Weiner: J. A. M. A. 112: 796, 1939.

13. Elman, R.: Proc. Soc. Exper. Biol. and Med. 37: 437, 1937.